administering to a mammalian subject having an abnormal brain region an in vivo activator of calcium-activated potassium channel, said activator being an activator of soluble guanylyl cyclase, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and

administering the medicant to the subject, simultaneously or substantially simultaneously with the activator, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

17.(Amended) The method of Claim 13, wherein the viral vector is a therapeutic adenoviral vector or herpes simplex virus vector.

18.(Amended) The method of Claim 1, wherein administering the activator is by intravenous or intra-arterial infusion or injection.

19.(Amended) The method of Claim 1, wherein administering the activator is by intracarotid infusion or injection.

20.(Amended) The method of Claim 1, wherein the activator is administered to the mammalian subject by a bolus injection.

21.(Amended) The method of Claim 1, wherein the activator is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

22.(Amended) The method of Claim 21, wherein the activator is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

23.(Amended) The method of Claim 1, wherein the activator is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu g\ kg^{-1}\ min^{-1}$ for up to about 30 minutes.

C5 cont'd

24.(Amended) The method of Claim 23, wherein the activator is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu g\ kg^{-1}\ min^{-1}$.

C6

48.(Twice Amended) A method of delivering a medicant to a malignant tumor in a mammalian subject, comprising:

administering to a mammalian subject having a malignant tumor an in vivo activator of calcium-activated potassium channel, said activator being an activator of soluble guanylyl cyclase, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the malignant tumor; and

administering the medicant to the subject, simultaneously or substantially simultaneously with the activator, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

C7

64.(Amended) The method of Claim 60, wherein the viral vector is a therapeutic adenoviral vector or herpes simplex virus vector.

65.(Amended) The method of Claim 48, wherein administering the activator is by intravenous or intra-arterial infusion or injection.

66.(Amended) The method of Claim 48, wherein administering the activator is by intracarotid infusion or injection.

67.(Amended) The method of Claim 48, wherein the activator is administered to the mammalian subject by a bolus injection.

68.(Amended) The method of Claim 48, wherein the activator is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

69.(Amended) The method of Claim 68, wherein the activator is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

70.(Amended) The method of Claim 48, wherein the activator is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu g\ kg^{-1}\ min^{-1}$ for up to about 30 minutes.

71.(Amended) The method of Claim 70, wherein the activator is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu g\ kg^{-1}\ min^{-1}$.

135. (Twice Amended) A pharmaceutical composition comprising a combination of an in vivo activator of calcium-activated potassium channel, said activator being an activator of soluble guanylyl cyclase, formulated in a pharmaceutically acceptable solution together with a medicant for delivery by intravascular infusion or injection into a mammal.

136.(Amended) The pharmaceutical composition of Claim 135, wherein the solution is formulated to deliver a dose rate of about 0.075 to 1500 micrograms of the activator per kilogram body mass in a pharmaceutically acceptable fluid volume over a maximum of about thirty minutes.

137. The pharmaceutical composition of Claim 135, wherein the solution is formulated to deliver a dose rate of about 0.075 to 150 micrograms of the activator per kilogram body mass in a pharmaceutically acceptable fluid volume over a period of up to thirty minutes.

C9

150.(Amended) The method of Claim 146, wherein the viral vector is a therapeutic adenoviral vector or herpes simplex virus vector.

C10

153.(Twice Amended) A kit for enhancing the delivery of a medicant to an abnormal brain region and/or to a malignant tumor, comprising:

an in vivo activator of calcium-activated potassium channel, said activator being an activator of soluble guanylyl cyclase; and

instructions for using the activator for enhancing the delivery of a medicant to an abnormal brain region or to a malignant tumor.

Please add new Claims 162-189 as follows.

C11

--162.(New) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising:

administering to a mammalian subject having an abnormal brain region an activator of soluble guanylyl cyclase selected from the group consisting of YC-1 and a NONOate, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and

administering the medicant to the subject, simultaneously or substantially simultaneously with the activator, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

163.(New) The method of Claim 162, wherein the NONOate is diethylamine-NONOate, diethylene triamine-NONOate, dipropylenetriamine-NONOate, spermine-NONOate, propylamino-propylamine-NONOate, MAHMA-NONOate, piperazi-NONOate, proli-NONOate, sulfo-NONOate, Angelis salt, or sulfite NONOate.

164.(New) The method of Claim 162, wherein administering the activator is by intravenous or intra-arterial infusion or injection.

165.(New) The method of Claim 162, wherein administering the activator is by intracarotid infusion or injection.

166.(New) The method of Claim 162, wherein the activator is administered to the mammalian subject by a bolus injection.

167.(New) The method of Claim 162, wherein the activator is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

168.(New) The method of Claim 167, wherein the activator is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

169.(New) The method of Claim 162, wherein the activator is administered to the mammalian subject at a dose rate of about 0.075 to about 100 μg kg-1 min-1 for up to about 30 minutes.

170.(New) The method of Claim 169, wherein the activator is administered to the mammalian subject at a dose rate of about 0.075 to about 15 μg kg-1 min-1 for up to about 30 minutes.

171.(New) The method of Claim 162, wherein said mammal is a human, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit.

172.(New) The method of Claim 162, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent,

anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

173.(New) The method of Claim 172, wherein the diagnostic agent is an imaging or contrast agent.

174.(New) The method of Claim 172, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

175.(New) The method of Claim 162, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor-β, cisplatin, carboplatin, tumor necrosis factor-α, methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

176.(New) The method of Claim 175, wherein the viral vector is a therapeutic adenoviral or herpes simplex virus vector.

177.(New) The method of Claim 162, wherein the abnormal brain region is a glioma or ischemic brain region.

178.(New) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising:

administering to a mammalian subject having an abnormal brain region a NONOate, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and

administering the medicant to the subject, simultaneously or substantially simultaneously with the NONOate, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

179.(New) The method of Claim 178, wherein the NONOate is diethylamine-NONOate, diethylene triamine-NONOate, dipropylenetriamine-NONOate, spermine-NONOate, propylamino-propylamine-NONOate, MAHMA-NONOate, piperazi-NONOate, proli-NONOate, sulfo-NONOate, Angelis salt, or sulfite NONOate.

180.(New) The method of Claim 178, wherein administering the NONOate is by intravenous or intra-arterial infusion or injection.

181.(New) The method of Claim 178, wherein administering the NONOate is by intracarotid infusion or injection.

182.(New) The method of Claim 178, wherein the NONOate is administered to the mammalian subject by a bolus injection.

183.(New) The method of Claim 178, wherein said mammal is a human, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit.

184.(New) The method of Claim 178, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.